REMARKS

Claims 85 and 86 are pending in the application.

- Claims 87 – 90 are objected to for not having proper claims identifiers.
- Claims 85 is rejected under 35 USC 112, second paragraph (indefiniteness).
- Claims 85 and 86 are rejected under 35 USC 112, second paragraph (enablement).
- Claims 85 and 86 are rejected under 35 USC 102(b).

Rejection under USC 35, 112, second paragraph (Indefiniteness)

The Examiner has rejected Claim 85 as not being indefinite for failing to particularly point out and directly claim the subject matter which applicant regards as his invention. Specifically, the Examiner did not find the Applicant's previous arguments persuasive because 1) the reference provided by the Applicant was undated and 2) Examiner provides two references allegedly showing that the claims limitation is "repugnant within the art." Applicant vigorously traverses the rejection.

First, Applicant has provided a publication demonstrating the physiological concentration of albumin as known to those of skill in the art. Applicant submitted with the previous Response (dated June 13, 2008) evidence of the physiological concentration of albumin in a human. Examiner states that "no date is assigned to the reference or other indication that this is a teaching that was known in the art at the time of filing." Pending Action, page 3. Applicant respectfully submits that unless Examiner can provide a showing that the physiological level of albumin changed between pre-filing and post-filing of the present application then the reference is more than adequate to support Applicant's claim of the physiological concentration of albumin in a human.

Second, Examiner has grossly mischaracterized the references cited in the pending Action. The cited Bohrmann reference does not teach the concentration of albumin as "an order of magnitude off from the concentration defined in Claim 86." Pending Action, page 3. The concentration cited in Bohrmann of 644 μM equals 44.4 mg/ml which is well within the concentration of albumin accepted by those in the art and consistent with the reference that the Applicant had provided.

Third, the cited Biere reference does not teach "physiological concentrations of albumin as defined as nanomolar concentrations." Pending Action, page 3. Rather, the Biere reference teaches the concentration of amyloid beta-peptide as nanomolar concentrations.

Thus, based on the art provided by the Examiner, the claimed element of concentration of "up to 60 mg/ml human serum albumin" was known to those of skill in the art at the time of the invention.

Rejection under USC 35, 112, first paragraph (Enablement)

The Examiner has rejected Claims 85 and 86 as containing subject matter that is not described in the specification in such a way as to enable one skilled in the art to which it pertains. In particular, the Examiner states:

> ... the specification, while being enabling for an *in vitro* method of forming an immune complex comprising contacting beta-amyloid with a specific antibody in the present of human serum albumin, does not reasonably provide enablement for the method practiced *in vivo*. Office Action mailed 7/31/2007, page 4.

In particular, Examiner states, "while being enabling for an *in* vitro method of forming an immune complex comprising contacting beta-amyloid with a specific antibody in the presence of human serum albumin and detecting the immune complex, does not reasonably provide enablement for the method practiced *in vivo*." Office Action mailed 9/10/2008, page 4.

Specification is Enabling for Practice of the Invention *in vivo*

Applicant respectfully traverses the rejection and submits that the specification as filed provides support for the practice of the present invention *in vivo*. Examiner's attention is directed towards paragraphs [0087], [0088] and Table 7 of the pending specification **wherein an *in vivo* use of the presently claimed invention is taught**. In this example, a murine model system is used to demonstrate that an antibody specific for an epitope of beta-amyloid forms an immune complex with beta-amyloid in the presence of physiological levels of serum albumin, thereby showing the "sequestering free beta-amyloid" *in vivo* (see, paragraph [0088] of the pending specification). Animal model systems are acceptable support for a method if the animal model system is accepted in the art as correlating with the claimed method of the invention. MPEP 2104.02. A rigorous correlation is not required.

> [B]ased upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative evidence. (Citations omitted.). *Cross v. Iizuka*, 753 F.2d 1040, 1050, 224 USPQ 739, 747 (Fed. Cir. 1985)

And, "Since the initial burden is on the Examiner to give reasons for the lack of enablement, the examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example." MPEP 2164.02. Examiner has failed to provide any such reasons in this or any prior Action.

Examiner states that Claims 85 and 86, as written, do not "provide guidance as to an *in vivo* method of detection for the immune complex." Pending Action, page 6. Applicants submit that the experiment described in paragraph [0088] of the pending specification provides this support ("... demonstrating the antibody can effectively bind Aβ in an experimental animal.") However, and without necessarily acquiescing to the Examiner's reasoning, Applicants have amended Claims 85 and 86 to recite "d) removing a sample from the incubation mixture of step c) and detecting the immune complex of beta-amyloid and antibody specific for a beta-amyloid epitope in the presence of physiological levels of human serum albumin" [Claim 85] or "... in the presence of up to 60 mg/ml of human serum albumin" [Claim 86]. These amendments essentially make the last step of Claims 85 and 86 *in vitro* steps. Therefore, Applicant submits that the specification as filed provides support for the pending claims as amended and respectfully requests that the rejection be withdrawn.

Applicant Addresses Examiner's Comments in Action dates 09/10/2008

The Examiner states in the Action dated 09/10/2008 that the pending claims are not enabled because "[g]iven the discrepancies as to the definition of a physiological level of serum albumin, and the rapid rate of turnover of free amyloid within the serum, and without specific guidance within the instant specification as to how to perform methods of detecting an immune complex within serum *in vivo*, one of ordinary skill in the art would have to perform undue experimentation in order to perform the last step of the method and sue the invention to the full scope of the claims." Pending Action, page 8.

1) The "discrepancies" as to the definition of physiological levels of serum albumin are addressed effectively above. 2) The Examiner quotes page 26 of the pending specification ("raises concern that [plasma] bound albumin will interfere with antibody binding") to make the argument that the art was unpredictable at the time of filing. Applicant submits that the quoted passage was taken out of context. Later in the same paragraph it is taught that binding "was unaffected by the presence of human serum albumin (HSA) at 60 mg/ml" thereby indicating that the bound albumin **did not** interfere with antibody binding. 3) The claims have been amended to limit the performance of the detection step *in vitro*.

Rejection under USC 35, 102(b)

Examiner has rejected Claims 85 and 86 under USC 35, 102(b) as being anticipated by Biere, *et al.* Applicant respectfully disagrees.

In order for a reference to be anticipatory the reference must teach every element of the claimed invention. MPEP 2131. Examiner states that the cited reference teaches that ~89 % of beta-amyloid is bound to albumin. Examiner states that the cited article teaches running the beta-amyloid:albumin complex on a non-denaturing gel and then performing a Western blot assay with anti-beta-amyloid antibody. Importantly, however, the cited reference makes no teaching of the concentration of albumin in the context of the Western blot assay where the immune complex between beta-amyloid and an anti-beta-amyloid antibody is formed.

Examiner continues by stating the Biere, *et al.*, teaches that "such an immune complex can form in the presence of physiological concentrations of albumin as defined as nanomolar concentrations (pg. 32916, last paragraph)." However, Examiner mischaracterizes the reference. The reference teaches the beta-amyloid, "when incubated in fresh human plasma at physiological (nanomolar) concentrations bind to certain plasma proteins [*i. e.*, albumin]." The cited reference does not teach the formation of an immune complex between beta-amyloid and an antibody specific fro a beta-amyloid epitope in the presence of physiological levels of human serum albumin or in the presence of up to 60 mg/ml human serum albumin, as is claimed in the present invention.

It is extremely unlikely that the concentration of serum albumin in the context a Western blot assay is the same as in the physiological state. Since concentration is a function of volume, one would need to extrapolate the concentration of albumin in the context of the Western blot based on the albumin present in the volume of solution present at the point of interaction between the antigen and antibody. The Examiner states that the "Applicant's claims do not require that this step be performed in the presence of physiological albumin." Pending Action, page 10. However, without necessarily agreeing with the Examiner arguments, Applicants have amended the pending claims to recite "d) removing a sample from the incubation mixture of step c) and detecting the immune complex of beta-amyloid and antibody specific for a beta-amyloid epitope in the presence of physiological levels of human serum albumin" [Claim 85] or "... in the presence of up to 60 mg/ml of human serum albumin" [Claim 86]. In view of these amendments, Applicants respectfully submit that the pending claims are not anticipated by Biere, *et al.*, and respectfully request the withdrawal of the pending rejection and allowance of the claims.

Summary

In light of the above Response, the passing of the subject patent application to allowance is respectfully requested.

Respectfully submitted,

Kevin M. Farrell
Attorney for Applicants
Registration No. 35,505
(603) 433-6300

Portsmouth, NH
Date: 11/9/09